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Pathways in Prevention: Addressing Seasonal Influenza in Older Adults

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Pathways in Prevention: Addressing Seasonal Influenza in Older Adults” is sponsored by Seqirus.

Here’s your host, Dr. Jennifer Caudle.

Dr. Caudle:
It’s an unfortunate reality that adults 65 years and older bear the greatest burden of severe disease from influenza, accounting for 70-90% of seasonal flu-related deaths in the United States, every single year. For this reason, it’s critically important to ask ourselves, what can we do to better prevent seasonal influenza infections in older adults? More thoughts on that and other practical questions to come on today’s program.

This is ReachMD, and I’m your host, Dr. Jennifer Caudle, and joining me in this important discussion is Dr. Archana Chatterjee, Dean of the Chicago Medical School and Vice-President for Medical Affairs at Rosalind Franklin University of Medicine and Science. Dr. Chatterjee, thank you so much for being here today.

Dr. Chatterjee:
Thank you, Dr. Caudle. I’m delighted to join you for this discussion.

Dr. Caudle:
Now, to start, let’s get a better scope of the various factors that influence this heavy disease burden for older adults. What do we need to keep top of mind, Dr. Chatterjee?

Dr. Chatterjee:
Well, there are several factors we need to take into consideration here. Let’s start with this patient population itself, because adults who are 65 years or older are more vulnerable to age-related immunosenescence and comorbidities which can increase the risk of reduced immune response to flu vaccines. Then we need to consider the strain of influenza, namely whether there’s a match between a vaccine strain and the circulating strain. We know that antigenic mismatch can lead to reduced vaccine effectiveness, so this is an important factor to keep in mind. In adults who are 65 years or older, the type of vaccine also needs to be taken into account, since conventional influenza vaccines may offer limited protection, in the efficacy range of 16-64%. Lastly, there’s the impact of surveillance systems. Not all sufferers of influenza seek medical attention, so we don’t get a complete real-time picture of the changes to disease burden in older adults from one region to another, or from one time period to another, and that creates a sort of blind spot for us, from a public health perspective. So clearly, with respect to reducing disease burden, we need a combination of good surveillance for burden targeting and vaccines capable of broader immune responses to help protect these patients against influenza.

Dr. Caudle:
And if we consider this issue at the molecular level, what do we know about the effects of aging on the immune system, and in particular, how getting older impacts infection rates and outcomes?

Dr. Chatterjee:
There are several components of both innate and adaptive immune systems that change in older adults. With the innate immune system, immune cells in adults at or beyond 65 years of age have reduced functional capacity, as in diminished ability to uptake antigen at the site of the injection, and an impaired ability to induce specific immunogenic response.

And also, adaptive immunity is deregulated in older adults, presenting as lowered ability to elicit an immunogenic memory response to newly introduced antigens, which impairs cytokine production. But it's really important to keep in mind that while all of these effects on the aging immune system have a negative impact on vaccine effectiveness, they also have ramifications on infection rates for these patients, and that takes shape in three ways: increased susceptibility to infection, increased severity of infection, and increased risk of hospitalization, which carries with it a greater risk of disability, reduced quality of life, and increased mortality rate.

Dr. Caudle:
So, let's focus now on vaccinations, because despite the challenges mentioned earlier with vaccination responses in older adults, annual vaccination against seasonal flus still remains the best primary weapon. But what's the impact of that weapon? Can you speak to its value on a macroscale?

Dr. Chatterjee:
I completely agree, Dr. Caudle, that vaccines remain the best defense against influenza. The evidence supporting their value is pretty compelling. For example, it's estimated that for the 2019-2020 influenza season, influenza vaccination prevented approximately 8 million influenza illnesses, 105,000 influenza hospitalizations and about 6,300 deaths.

Dr. Caudle:
Now, let's stay on that theme of impact and talk about the new technologies at the forefront of influenza prevention. Can you walk us through these approaches?

Dr. Chatterjee:
Sure. So there are different advanced technologies – cell-based, adjuvanted, high-dose and recombinant vaccines. Cell-based vaccines are subunit vaccines that utilize influenza virus, prepared and propagated in a continuous cell line, that do not contain egg protein. The immunogenicity and reactogenicity of these vaccines are similar to that of standard conventional vaccines. Adjuvanted vaccines, on the other hand, are prepared with MF59 adjuvant, which is a squalene-based oil-in-water emulsion and are combined with antigen. These vaccines elicit a more robust immune response compared to standard conventional vaccines, which is particularly important for adults 65 years and older since they are more vulnerable to age-related immunosenescence and comorbidities, increase the risk of reduced immune response to flu vaccines. High-dose vaccines are split Virion vaccines. As their name implies, they have a much greater amount of antigen than the standard dose – about four times greater to be specific. And, as one might expect, this higher dose vaccine approach elicits a stronger immune response than its conventional vaccine counterpart. Lastly, we have recombinant vaccines, which contain recombinant hemagglutinin proteins, prepared from a serum-free derived insect cell line. So they stand apart in this way, but their immunogenicity and reactogenicity still appear to be in the same range as conventional vaccines.

Dr. Caudle:
For those of you who are just joining in, this is ReachMD, and I'm your host, Dr. Jennifer Caudle, and with me today is Dr. Archana Chatterjee, to talk about current influenza vaccines, and how we can improve our infection prevention efforts in older patients.

So Dr. Chatterjee, you've given us a great rundown of conventional versus advanced vaccine technologies. So, let's focus on adjuvanted vaccines now, given the immune response they elicit. How do adjuvants change the immunization dynamic against seasonal flu, especially for older adults?

Dr. Chatterjee:
As I mentioned earlier, adjuvants such as MF59 enhance the magnitude, breadth and persistence of immune responses. But I don't think that in itself fully explains why adjutants matter for seasonal influenza or pandemic influenza. So let's look at a few reasons for making immune response a priority here.

First, we know that individuals with a naïve or weakened immune system have a diminished response to vaccines, and we covered some of the ways this develops at the cellular level over time. Second, vaccine antigens may not exactly match the circulating strain of influenza, and when you combine that with a suboptimal immune response in adults 65 years and older, it really takes down our ability to prevent flu infections in these patients. And finally, it's unfortunate but true that vaccine antigens can run into short supply with limited access, especially during a pandemic. So, having advanced methods that may leverage less antigen when combined with adjutants like MF59 helps vaccine developers avoid that shortfall.

Dr. Caudle:
And on that last point, let's focus on this adjuvant, MF59. What can you tell us about it?

Dr. Chatterjee:
MF59 is an oil-in-water emulsion composed of squalene, which is a biodegradable and biocompatible oil. Squalene is actually an intermediate precursor in the cholesterol biosynthetic pathway, so it's synthesized naturally in the liver, and also comes from dietary

sources. MF59 amplifies the signal to the local immune system by recruiting immune cells, starting right at the site of the injection. Remember, for adults over the age of 65, the immune cascade is muted, so with the addition of MF59 to the seasonal influenza vaccine, the antigen re-uptake increases within these immune cells, and they differentiate into antigen-presenting cells, or APCs, which then migrate to the lymph nodes and activate T-cell and B-cell expansions that foster a robust immune response. The mechanism of action for MF59 has been investigated, and what's been elucidated is that when MF59 is added to the antigen contained in the influenza vaccine, it enhances the immune response in a few complimentary ways: first, by increasing the magnitude of circulating antibody levels, using standardized measures for antibody titers; second, by adding to the breadth of the vaccine by promoting cross-reactive antibody production; and third, by increasing the persistence or duration of functional antibodies.

Dr. Caudle:
Well, that was a great mechanistic review, Dr. Chatterjee. Thank you so much for that. You know, now as we come to the end of our program today, let me open the floor to you for any additional thoughts or takeaways you may want to impart to our audience, based on everything we covered.

Dr. Chatterjee:
Thanks, Dr. Caudle. Above and beyond anything else, I want to reiterate how important it is for us to prioritize reducing the burden of influenza on older adults, who we know bear the brunt of that burden throughout most flu seasons. Vaccines clearly represent our best defense in this fight, now more than ever, but we need to consider different types of vaccines if we are going to improve immune responses and clinical outcomes for these patients. We talked a fair amount about adjuvanted flu vaccines as an advanced option, and again, why I think this is so important comes back to enhancing those three key aspects of the immune response: its magnitude, its breadth and its persistence. And lastly, I want to reiterate that our understandings around how aging affects the immune system, and these proposed mechanisms behind adjuvants such as MF59 to enhance immunogenicity towards flu vaccines are ongoing and continually evolving, and they have to be, because we are up against a virus that's constantly evolving as well.

Dr. Caudle:
Well, considering everything we now know about seasonal flu and its heavy impacts on patient populations such as those 65 years of age and older, this renewed focus on preventative strategies is not only welcome, but it's critically needed. I'd like to thank my guest, Dr. Archana Chatterjee, for helping us better understand the current and emerging options to defend our older patients population against this infectious disease. Dr. Chatterjee, it was great speaking with you today.

Dr. Chatterjee:
And it was a pleasure to speak with you as well, Dr. Caudle. Thank you.

Announcer:
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